

CLAIMS

1. A method of treating a patient having an immunologic disorder, comprising:
 - (a) administering to the patient a therapeutically effective amount of a BAFF (B cell activating factor belonging to the TNF family) antagonist at least once or at one or more intervals of less than N weeks;
 - (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and
 - (c) repeating steps (a) and (b) at least once; wherein N is 8, 9, 10, 11, or 12.
2. The method of claim 1, wherein the administration of step (a) comprises an interval of 1, 2, 3, 4, 5, 6, or 7 weeks.
3. The method of claim 1, wherein the BAFF antagonist is administered in step (a) 2, 3, 4, 5, 6, or 7 times a week.
4. The method of claim 1, wherein the administration is discontinued in step (b) for 12, 18, 24, 30, 36, 42, 48 weeks or longer.
5. The method of claim 1, wherein at the beginning of the treatment the patient has one or more of:
 - (i) proteinuria of 1 g per a 24-hour period or higher;
 - (ii) serum creatinine levels of about 1 mg/dl or higher;
 - (iii) creatinine clearance levels of 97 ml/min or lower;
 - (iv) blood urea of 20 mg/dl or higher;
 - (v) abnormal titer of autoantibodies in the serum; and
 - (vi) peripheral blood B cell count of 700 cells/ μ l.

6. The method of claim 5, wherein the patient is human.
7. The method of claim 1, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to inhibit autoantibody titer.
8. The method of claim 1, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce B cell hyperplasia.
9. The method of claim 1, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce cardiac inflammation.
10. The method of claim 1, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to improve renal function.
11. The method of claim 10, wherein the renal function is one or more of: pressure filtration, selective reabsorption, tubular secretion, and systemic blood pressure regulation.
12. The method of claim 1, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce progression of renal fibrosis.
13. The method of claim 1, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce lymphocyte infiltration in the kidneys.
14. The method of claim 1, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce lymphadenopathy.
15. The method of claim 1, wherein the immunologic disorder is an autoimmune disorder.
16. The method of claim 15, wherein the autoimmune disorder is systemic lupus erythematosus.

17. The method of any one of claims 1-16, wherein the medicament is LymphoStat-B™.

18. The method of any one of claims 1-16, wherein the BAFF antagonist is BAFF-specific.

19. The method of claim 18, wherein the BAFF antagonist is selected from the group consisting of a soluble BAFF receptor, an anti-BAFF antibody and an anti-BAFFR antibody.

20. The method of claim 19, wherein the BAFF receptor is selected from the group consisting of BAFFR, BCMA (B cell maturation antigen) and TACI (transmembrane activator and cyclophilin ligand interactor).

21. The method of claim 20, wherein the soluble BAFFR comprises the peptide of SEQ ID NO:5.

22. The method of claim 19, wherein the soluble BAFF receptor comprises a BAFF-binding domain of BAFFR.

23. The method of claim 20, wherein the soluble BAFFR is human.

24. The method of claim 20, wherein the soluble BAFFR lacks the sequence of SEQ ID NO:6.

25. The method of claim 22, wherein the BAFF-binding domain of BAFFR has an amino acid sequence as set out:

- (a) from amino acid 27 to amino acid 32 of SEQ ID NO:1;
- (b) from amino acid 18 to amino acid 43 of SEQ ID NO:1;
- (c) from amino acid 13 to amino acid 50 of SEQ ID NO:1;
- (d) from amino acid 3 to amino acid 73 of SEQ ID NO:1; or
- (e) amino acid 2 to amino acid 62 of SEQ ID NO:3.

26. The method of claim 22, wherein the BAFF-binding domain of BAFFR is fused to a constant region of an immunoglobulin.

27. The method of claim 26, wherein the immunoglobulin is IgG₁ or IgG₄.

28. The method of claim 26, wherein the constant region of an immunoglobulin comprises an Fc portion.

29. The method of claim 28, wherein the BAFFR-Fc comprises (a) an amino acid sequence as set out in SEQ ID NO:2 or (b) an amino acid sequence as set out in SEQ ID NO:4.

30. A method of treating a patient having an autoimmune disorder, comprising:

(a) administering to the patient a therapeutically effective amount of a BAFF-specific antagonist at least once or at one or more intervals of less than N weeks;

(b) temporarily discontinuing the administration of step (a) for N weeks or longer; and

(c) repeating steps (a) and (b) at least once; thereby treating the autoimmune disorder, and wherein N is 8, 9, 10, 11, or 12.

31. A method of reducing autoantibody titer in a patient, comprising:

(a) administering to the patient a therapeutically effective amount of a BAFF-specific antagonist at least once or at one or more intervals of less than N weeks;

- (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and
- (c) repeating steps (a) and (b) at least once; thereby reducing autoantibody titer, and wherein N is 8, 9, 10, 11, or 12.

32. A method of inhibiting generation of pathogenic B cells in a patient, comprising:

- (a) administering to the patient a therapeutically effective amount of a BAFF-specific antagonist at least once or at one or more intervals of less than N weeks;
- (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and
- (c) repeating steps (a) and (b) at least once; thereby inhibiting generation of pathogenic B cells, and wherein N is 8, 9, 10, 11, or 12.

33. The method of claim 32, wherein the pathogenic B cells are IgM⁺ IgD⁺.

34. The method of any one of claims 30-33, wherein the BAFF-specific antagonist is a soluble form of BAFFR.

35. The method of any one of claims 30-33, wherein the BAFF-specific antagonist is an anti-BAFF-antibody.

36. Use of a BAFF antagonist for preparation of a medicament for treatment of an immunologic disorder, wherein the treatment regimen comprises:

- (a) administering a therapeutically effective amount of a BAFF (B cell activating factor belonging to the TNF family) antagonist at least once or at one or more intervals of less than N weeks;
- (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and
- (c) repeating steps (a) and (b) at least once; wherein N is 8, 9, 10, 11, or 12.

37. The use of claim 36, wherein the administration of step (a) comprises an interval of 1, 2, 3, 4, 5, 6, or 7 weeks.

38. The use of claim 36, wherein the BAFF antagonist is administered in step (a) 2, 3, 4, 5, 6, or 7 times a week.

39. The use of claim 36, wherein the administration is discontinued in step (b) for 12, 18, 24, 30, 36, 42, 48 weeks or longer.

40. The use of claim 36, wherein at the beginning of the treatment the patient has one or more of:

- (i) proteinuria of 1 g per a 24-hour period or higher;
- (ii) serum creatinine levels of about 1 mg/dl or higher;
- (iii) creatinine clearance levels of 97 ml/min or lower;
- (iv) blood urea of 20 mg/dl or higher;
- (v) abnormal titer of autoantibodies in the serum; and
- (vi) peripheral blood B cell count of 700 cells/ μ l.

41. The use of claim 40, wherein the patient is human.

42. The use of claim 36, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to inhibit autoantibody titer.

43. The use of claim 36, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce B cell hyperplasia.
44. The use of claim 36, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce cardiac inflammation.
45. The use of claim 36, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to improve renal function.
46. The use of claim 45, wherein the renal function is one or more of: pressure filtration, selective reabsorption, tubular secretion, and systemic blood pressure regulation.
47. The use of claim 36, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce progression of renal fibrosis.
48. The use of claim 36, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce lymphocyte infiltration in the kidneys.
49. The use of claim 36, wherein the therapeutically effective amount of the BAFF antagonist is sufficient to reduce lymphadenopathy.
50. The use of claim 36, wherein the immunologic disorder is an autoimmune disorder.
51. The use of claim 50, wherein the autoimmune disorder is systemic lupus erythematosus.
52. The use of any one of claims 36-51, wherein the medicament is LymphoStat-B™.

53. The use of any one of claims 36-51, wherein the BAFF antagonist is BAFF-specific.

54. The use of claim 53, wherein the BAFF antagonist is selected from the group consisting of a soluble BAFF receptor, an anti-BAFF antibody, and an anti-BAFFR antibody.

55. The use of claim 54, wherein the soluble BAFF receptor is selected from the group consisting of BAFFR, BCMA (B cell maturation antigen) and TACI (transmembrane activator and cyclophilin ligand interactor).

56. The use of claim 55, wherein the BAFFR comprises the peptide of SEQ ID NO:5.

57. The use of claim 54, wherein the soluble BAFF receptor comprises a BAFF-binding domain of BAFFR.

58. The use of claim 55, wherein the BAFFR is human.

59. The use of claim 55, wherein the BAFFR lacks the sequence of SEQ ID NO:6.

60. The use of claim 57, wherein the BAFF-binding domain of BAFFR has an amino acid sequence as set out:

- (a) from amino acid 27 to amino acid 32 of SEQ ID NO:1;
- (b) from amino acid 18 to amino acid 43 of SEQ ID NO:1;
- (c) from amino acid 13 to amino acid 50 of SEQ ID NO:1;
- (d) from amino acid 3 to amino acid 73 of SEQ ID NO:1; or
- (e) amino acid 2 to amino acid 62 of SEQ ID NO:3.

61. The use of claim 57, wherein the BAFF-binding domain of BAFFR is fused to a constant region of an immunoglobulin.

62. The use of claim 61, wherein the immunoglobulin is IgG₁ or IgG₄.

63. The use of claim 61, wherein the constant region of an immunoglobulin comprises an Fc portion.

64. The use of claim 63, wherein the BAFFR-Fc comprises (a) an amino acid sequence as set out in SEQ ID NO:2 or (b) an amino acid sequence as set out in SEQ ID NO:4.

65. Use of a BAFF-specific antagonist for preparation of a medicament for treatment of an autoimmune disorder, wherein the treatment regimen comprises:

(a) administering to the patient a therapeutically effective amount of a BAFF-specific antagonist at least once or at one or more intervals of less than N weeks;

(b) temporarily discontinuing the administration of step (a) for N weeks or longer; and

(c) repeating steps (a) and (b) at least once; thereby treating an autoimmune disorder, and wherein N is 8, 9, 10, 11, or 12.

66. Use of a BAFF-specific antagonist for preparation of a medicament for reducing autoantibody titer, wherein the treatment regimen comprises:

- (a) administering to the patient a therapeutically effective amount of a BAFF-specific antagonist at least once or at one or more intervals of less than N weeks;
- (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and
- (c) repeating steps (a) and (b) at least once; thereby reducing autoantibody titer, and wherein N is 8, 9, 10, 11, or 12.

67. Use of a BAFF-specific antagonist for preparation of a medicament for inhibiting generation of pathogenic B cells, wherein the treatment comprises:

- (a) administering to a patient a therapeutically effective amount of a BAFF-specific antagonist at least once or at one or more intervals of less than N weeks;
- (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and
- (c) repeating steps (a) and (b) at least once; wherein N is 8, 9, 10, 11, or 12.

68. The use of claim 67; wherein the pathogenic B cells are IgM⁺ IgD⁺.

69. The use of any one of claims 65-68, wherein the BAFF-specific antagonist is a soluble form of BAFFR.

70. The use of any one of claims 65-68, wherein the BAFF-specific antagonist is an anti-BAFF-antibody.